Supplementary Information

Estimating the proportion of variation in susceptibility to schizophrenia captured by common SNPs

CONTENTS

Supplementary Table 1. Case-control studies comprising PGC-SCZ

Sub-set	Sample Cohort	Genotyping Platform	In PGC-SCZ GWAS Cases	In PGC-SCZ GWAS Controls	Used here Cases	Used here Controls
ISC	ISC-Aberdeen	Affymetrix 5.0	720	698	696	661
ISC	ISC-Cardiff	Affymetrix 6.0	527	609	518	597
ISC	ISC-Dublin	Affymetrix 6.0	270	860	264	838
ISC	ISC-Edinburgh	Affymetrix 6.0	368	284	360	279
ISC	ISC-London	Affymetrix 5.0 & 500K	518	491	516	491
ISC	ISC-Portugal	Affymetrix 5.0	346	215	324	189
ISC	ISC-SW1	Affymetrix 5.0	168	167	164	166
ISC	ISC-SW2	Affymetrix 6.0	390	229	378	224
ISC	Total		**3307**	**3553**	**3220**	**3445**
MGS	MGS	Affymetrix 6.0	**2679**	**2484**	**2571**	**2419**
OTH	SGENE-Bonn	Illumina 550K	474	1,304	475	1297
OTH	SGENE-CH	Illumina Human 610-Quad	482	457	476	450
OTH	SGENE-MUN	Illumina 300K	434	351	424	351
OTH	SGENE-TOP3	Affymetrix 6.0	248	351	244	348
OTH	SGENE-UCLA	Illumina 550K	704	631	695	623
OTH	Cardiff	Affymetrix 550K	472	2,934	465	2917
OTH	CATIE	Affymetrix 500K; Perlegen 164K	402	207	379	209
OTH	Zucker Hillside	Affymetrix 500K	192	190	138	112
OTH	Total		**3408**	**6425**	**3296**	**6307**
Total	PGC-SCZ		**9394**	**12462**	**9087**	**12171**

The case-control samples contributing to PGC-SCZ are described in detail in the Supplementary Material of Ripke *et al*[1]. All PGC-SCZ data sets underwent stringent quality control (QC) separately prior to imputation but using the same common parameters:

- Missing rate per SNP <0.05 (prior to sample removal below)
- Missing rate per individual <0.02
- Missing rate per SNP <0.02 (after sample removal above)
- Missing rate per SNP difference cases-controls <0.02
- SNP frequency difference to HapMap <0.15
- Hardy-Weinberg Equilibrium (H-W) test (controls) $p<10^{-6}$

The reduced numbers used here compared to the PGC-SCZ GWAS reflects more stringent selection of individuals who are unrelated in the classical sense, average relatioship (equation 2) < 0.05.

Supplementary Table 2. Pilot analyses using the ISC and MGS GWAS data; estimates of proportion of variance in liability explained by SNPs (h^2) **See Supplementary Note**

Analysis	Source	Genotypes	Cases	Controls	SNPs	LR	h^2 (s.e.)	h^2 (s.e.) Adjusted
ISC								
1	Baseline stringent QC	G	2,538	2,788	287,782	141	0.33 (0.03)	0.38 (0.03)
2	Extreme QC	G	2,538	2,788	196,322	100	0.27 (0.03)	0.32 (0.03)
3	In PGC-SCZ	I	3,220	3,445	915,354	165	0.28 (0.02)	0.30 (0.02)
4	In PGC-SCZ	G	3,220	3,445	192,477	146	0.26(0.02)	0.30 (0.02)
5	In PGC-SCZ ex London	I	2,704	2,954	915,354	138	0.31 (0.03)	0.33 (0.03)
MGS								
6	Baseline stringent QC	G	1,294	1,862	590,622	41	0.36 (0.06)	0.38(0.06)
7	Extreme QC	G	1,294	1,862	491,851	31	0.30(0.05)	0.32(0.06)
8	In PGC-SCZ	I	2,571	2,419	915,354	135	0.34 (0.03)	0.35 (0.03)
9	In PGC-SCZ	G	2,571	2,419	460,939	120	0.32 (0.03)	0.35 (0.03)

G: genotyped SNPs only; I imputed SNPs: LR: likelihood ratio test statistic; h^2 Adjusted estimate of proportion of variance in liability to schizophrenia explained by SNPs adjusted to account for incomplete linkage disequilibrium between causal variants and SNPs; SE standard error of h^2. NB All analyses include 4 ancestry principal components. In main text 20 ancestry principal components are used.

Supplementary Table 3. Estimated proportion of variance in liability attributable to SNPs on the X chromosome (h^2) **See Supplementary Note**

a) Bivariate analyses in which trait 1 comprises only male data and trait 2 comprises only female data

	Male h^2 (s.e.)	Female h^2 (s.e.)	r
PGC-SCZ Autosome	0.244 (0.013)	0.253 (0.019)	0.894 (0.058)
MGS-ISC Autosome	0.268 (0.032)	0.253 (0.045)	0.902 (0.139)
MGS-ISC X	0.008 (0.006)	0.010 (0.008)	0.909 (0.688)

ISC and MGS data sets combined, comprised 21380 genotyped SNPs on the X chromosome

b) Comparing equal variance vs. dosage compensation models

	LR	h^2 (s.e.)
Equal variance model (male variance = female variance)	7.64	0.009 (0.004)
dosage compensation model- female variance (male variance=2*female variance)	11.11	0.007 (0.002)

Supplementary Table 4. Estimated proportion of variance in liability (h^2) to schizophrenia explained by SNPs in CNS+ genes, other genes and not in genes.

	No. Genes	No. SNPs	~Mb	Mb as % of total	h^2 (s.e.)	h^2 as % of total (s.e.)
CNS+ genes	2725	195044	547	20[†]	0.07 (0.01)	31 (2)[†]
Other genes	14804	355562	1069	39	0.08 (0.01)	35 (2)
Not in genes		364748	1155	42	0.08 (0.01)	34 (2)
Total			2772	100	0.23	100

Estimates based on 915354 imputed SNPs; SE standard error of h^2. † The proportion 31 % (s.e. 2%) is significantly different to the proportion 20% p =7.6 x 10^{-8}.

Supplementary Table 5. Estimated proportion of variance in liability to schizophrenia explained by SNPs, partitioned by minor allele frequency (MAF), for a single analysis of all five MAF categories (Joint) or five individual analyses of each MAF bin.

MAF of SNPs	Number of SNPs	h^2 (s.e.) ISC (Joint)	MGS (Joint)	OTH (Joint)	PGC-SCZ (Joint)	PGC-SCZ (Separate)	PGC-SCZ (Proportion[a])
<0.1	158497	0.03 (0.02)	0.02 (0.02)	0.02 (0.01)	0.02 (0.01)	0.06 (0.01)	0.26 (0.04)
0.1 – 0.2	209466	0.05 (0.02)	0.05 (0.03)	0.07 (0.02)	0.05 (0.01)	0.12 (0.01)	0.52 (0.05)
0.2 – 0.3	191270	0.05 (0.02)	0.08 (0.03)	0.06 (0.02)	0.04 (0.01)	0.13 (0.01)	0.57 (0.05)
0.3 – 0.4	181782	0.07 (0.02)	0.12 (0.03)	0.06 (0.01)	0.06 (0.01)	0.13 (0.01)	0.57 (0.05)
0.4<	174339	0.07 (0.02)	0.03 (0.02)	0.05 (0.01)	0.05 (0.01)	0.11 (0.01)	0.48 (0.04)
sum	915354	0.27	0.30	0.26	0.22		

a. Proportion of the variance explained by all SNP (0.22) explained by SNPs in each MAF bin from the separate analyses

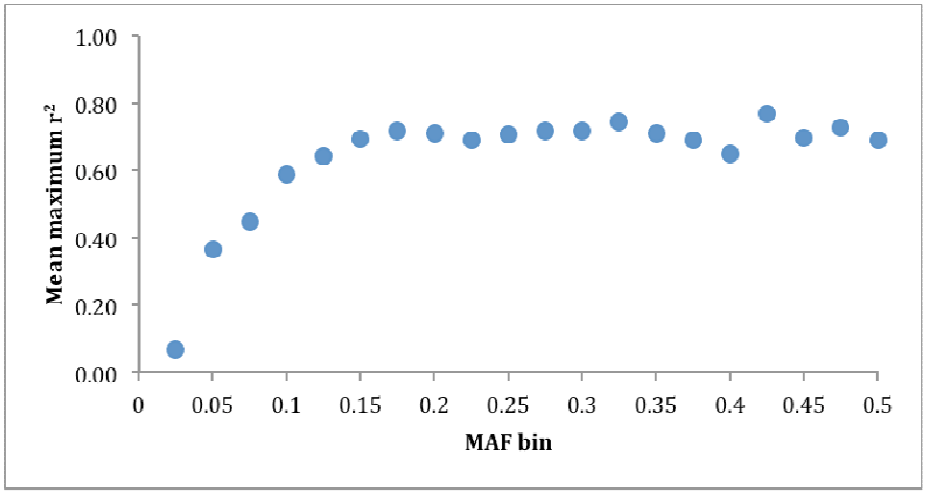
Supplementary Table 6. Estimated proportion of variance explained (h^2) using simulated data based on all PGC-SCZ imputed genotypes. **See Supplementary Note**

	All variance in liability associated with SNPs with MAF < 0.1				All variance in liability associated with SNPs across the MAF spectrum	
	Joint analysis	Joint analysis	Separate analysis	Separate proportion[a]	Joint analysis	Separate analysis
25% of variance in liability attributed to SNPs with MAF < 0.1						
< 0.1	0.25 (0.004)	Not included	0.25 (0.004)	1.00 (0.016)	0.05 (0.005)	0.08 (0.004)
0.1 - 0.2	0.00 (0.004)	0.06 (0.004)	0.07 (0.003)	0.28 (0.012)	0.05 (0.004)	0.12 (0.004)
0.2 - 0.3	0.00 (0.003)	0.01 (0.003)	0.04 (0.002)	0.16 (0.008)	0.05 (0.004)	0.13 (0.003)
0.3 - 0.4	0.00 (0.002)	0.01 (0.003)	0.03 (0.002)	0.12 (0.008)	0.05 (0.003)	0.12 (0.002)
0.4 –0.5	0.00 (0.002)	0.00 (0.003)	0.02 (0.002)	0.08 (0.008)	0.05 (0.002)	0.11 (0.002)
Total	0.25	0.08			0.25	
50% of variance in liability attributed to SNPs with MAF < 0.1						
< 0.1	0.50 (0.003)	Not included	0.50 (0.003)	1.00 (0.007)	0.08 (0.003)	0.16 (0.003)
0.1 - 0.2	0.00 (0.002)	0.13 (0.004)	0.14 (0.003)	0.28 (0.007)	0.12 (0.004)	0.26 (0.005)
0.2 - 0.3	0.00 (0.003)	0.02 (0.004)	0.08 (0.002)	0.16 (0.004)	0.10 (0.003)	0.26 (0.004)
0.3 - 0.4	0.00 (0.003)	0.01 (0.004)	0.06 (0.003)	0.12 (0.006)	0.10 (0.004)	0.25 (0.004)
0.4 –0.5	0.00 (0.003)	0.02 (0.003)	0.05 (0.003)	0.10 (0.006)	0.10 (0.004)	0.22 (0.004)
Total	0.50	0.18			0.50	
80% of variance in liability attributed to SNPs with MAF < 0.1						
< 0.1	0.80 (0.003)	Not included	0.80 (0.002)	1.00 (0.003)	0.14 (0.003)	0.28 (0.004)
0.1 - 0.2	0.00 (0.002)	0.21 (0.004)	0.24 (0.004)	0.30 (0.005)	0.18 (0.004)	0.42 (0.004)
0.2 - 0.3	0.00 (0.002)	0.05(0.003)	0.14 (0.003)	0.17 (0.004)	0.17 (0.004)	0.44 (0.002)
0.3 - 0.4	0.00 (0.002)	0.02 (0.004)	0.10 (0.004)	0.13 (0.005)	0.16 (0.005)	0.42 (0.003)
0.4 –0.5	0.00 (0.002)	0.02 (0.003)	0.09 (0.004)	0.11 (0.005)	0.15 (0.004)	0.37 (0.003)
Total	0.80	0.30			0.80	

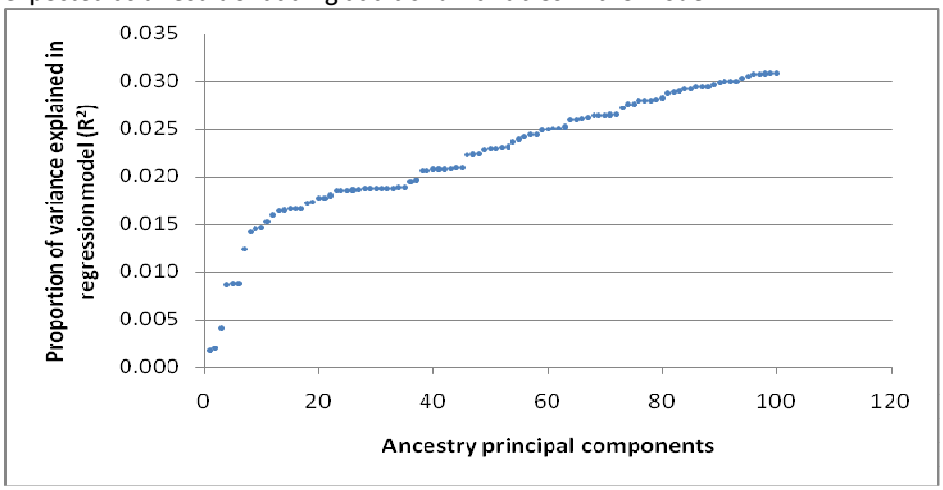
a.Proportion of the variance explained by all SNP (ie 0.25, 0.5 or 0.8) explained by SNPs in each MAF bin from the separate analyses. Values in parenthesis are standard errors of the mean estimates over 10 replicates.

SUPPLENTARY FIGURES.

Supplementary Figure 1. Mean maximum linkage disequilibrium r^2 measure between a random sample of SNPs in 1000G and SNPs on the Affymetrix 6.0 genotyping chip. We used genotype data from the 1000 genomes (1000G) project[2] to provide an estimate of the proportion of known variance in the genome explained by SNPs genotyped in the PGC-SCZ. We selected 10,000 autosomal SNPs ("target" SNPs) at random from the 37 million SNPs in European 1000G (381 samples); this random selection ensures that these target SNPs are unlikely to be in LD with each other. After excluding monomorphic SNPs, 4292 SNPs were assigned to MAF bins; 52% of these had frequency in the first MAF bin, defined as MAF < 0.025. We calculated the maximum LD r^2 between each target SNP and SNPs within ±1Mb about it included in the MGS genotyped SNP set (Affymetrix 6.0 ~460k SNPs) using European 1000G data. These results are consistent with those published using the pilot 1000G data[3].



Supplementary Figure 2. Proportion of variance explained from regression of case-control status on increasing numbers of ancestry principal components. Case control status is the dependent variable and sex and sample cohort were included as covariates. The principal components are entered in their eigenvalue order. The increase in R^2 with > 20 principal components is linear, an increase expected as a result of adding additional variables in the model.



SUPPLEMENTARY NOTE.

1) Notes on Supplementary Table 2

The purpose of Supplementary Table 2 is to demonstrate that the QC applied to the PGC-SCZ data did not introduce any bias which would inflate the estimates of variance explained by SNPs. To do this we made comparisons with our own QC and extensive original analyses of the ISC and MGS data sets. Those original analyses utilised plate/batch effects, information which was not available for the full PGC-SCZ data; our analyses confirmed that the PGC-SCZ QC procedure is unlikely to introduce inflated estimates of variance explained by SNPs.

ISC

Our preliminary analyses first used only genotyped SNPs from the ISC GWAS data set provided to us directly by the ISC, comprising 3,322 European individuals with schizophrenia and 3,587 controls (ancestry outliers had been excluded)[4]. To check that the estimated h^2 attributed to SNPs could not reflect systematic bias caused from batch effects or genotyping errors we investigated the impact of imposing extremely stringent QC thresholds. We excluded the ISC-London sample because cases and controls were genotyped on different platforms, for all other cohorts cases and controls were genotyped together. We also excluded subjects so that no pair of individuals had a genome-wide similarity coefficient (equation 2) > 0.05. We included genotyping plate as an additional random effect in the linear mixed model. The baseline stringent QC excluded SNPs if they had

- MAF < 0.01
- Missingness rate (MR) > 0.05
- H-W test p<0.0001

We compared the estimates h^2 to those obtained with extreme QC , defined as exclusion of SNPs with p<0.05 for

- the H-W test, including in any individual data set contributing to the for ISC
- the test for differential missingness of genotypes between cases and controls,
- two-locus QC test[5] applied in a very conservative way so that each SNP was explicitly paired and tested with each of 20 flanking markers.

The numbers of SNPs, cases and controls remaining after these QC steps are listed in the table. Comparison of the estimates of h^2 between analyses 1 and 2 shows a lower estimate, but not significantly so, when extreme QC is applied, implying that the variance detected is unlikely to be explained by genotyping artefacts. The extreme QC leads to a loss of SNPs so the reduced estimate of h^2 may reflect reduced LD between the genotyped SNPs and causal variants. In order to make fairer comparisons between alternatives because of the differing numbers of SNPs we adjusted the estimated variance to account for the imperfect LD between the genotyped SNPs and causal variants. The adjustment assumes that causal variants have allele frequency spectrum and LD patterns with genotyped SNPs similar to the allele frequency spectrum of, and LD patterns between, genotyped SNPs[6,7] used in the analysis. If the SNPs remaining in the extreme QC set were a random set of the SNPs in the baseline QC set, then the adjusted h^2 estimated from the two analyses would be the same. However, we noted that the extreme QC preferentially excluded low minor allele frequency (MAF) SNPs and so the variance captured by these SNPs could not be recovered by the adjustment.

In order to use the PGC-SCZ data we wished to confirm that neither the QC applied to PGC-SCZ data nor the use of imputed genotypes would introduce artefactual inflation of the estimates of h^2. We found that the adjusted estimate of variance explained for the ISC sample in PGC-SCZ was less in the ISC sample following our QC procedures (analysis 3 vs. analysis 1 and 2). The analyses differ in several ways (imputed v genotyped SNPs, QC on SNPs, QC on samples). In order to exclude

imputation as a source of bias we repeated analysis 3 using only the SNPs that survived PGC-SCZ QC and show that the adjusted estimate of variance explained is the same for genotyped as imputed SNPs (analysis 4 vs. 3). The number of SNPs in analysis 4 is fewer than that from our extreme QC procedure, but this likely reflects less extreme QC on samples. To investigate the impact of sample QC we excluded the ISC London sample from the PGC-SCZ ISC data (analysis 5), as this was the major difference between samples used in our analysis and the PGC analysis. The adjusted h^2 from this analysis is more in line with the estimates from analysis 1 and 2. We conclude that the sample PGC-SCZ QC steps do not introduce artefactual inflation of estimates.

MGS

Our second set of preliminary analyses used the MGS GWAS data set[9] with data on genotyped SNPs accessed with permission from dbGAP. Non-European ancestry outliers based on principal components were excluded. Samples genotyped on plates where the vast majority of samples were either cases or controls were excluded as were samples where the DNA was extracted from cell lines rather than blood, as this DNA source was highly confounded with case-control status. The numbers of SNPs, cases and controls remaining after these QC steps are listed in Supplementary Table 2. We repeated the analyses (1-4) undertaken for the ISC data set using the MGS data set and confirmed no upward biases resulting from using the PGC-SCZ QCed samples nor the imputed genotypes.

Importantly, our analyses demonstrate that the estimates of the proportion of variation in liability to schizophrenia that is tagged by common SNPs are fully consistent between two large independent case-controls studies. The analyses listed in Supplementary Table 2 justified the use of the full PGC-SCZ sample and imputed genotypes as reported in the main paper.

2) Notes on Supplementary Table 3

a) Although the point estimates of the variance explained by X chromosome SNPs is greater in females than in males, the difference is not significant. The variance explained by the X chromosome is consistent with its length (Figure 1). The correlation between the liabilities for schizophrenia based on SNP data from males and females is the same for the X chromosome as for autosomes.
b) The relationship matrix derived from SNPs in the X chromosome was simultaneously fitted with the relationship matrix derived from SNPs in autosomes. The likelihood ratio test statistic to test the null hypothesis that the variance is zero is significant and high for both the equal variance and dosage compensation models and it is difficult to distinguish between them with these data.

3) Notes on Supplementary Table 6

The simulations were conducted to provide insight into the observed results and aimed to establish if very common causal variants could be excluded. First we summarise the observed results:

i) Analysis of the PGC-SCZ data showed that SNPS with MAF > 0.4 explained 5% (s.e. 1%) of the variance in liability (Supplementary Table 5), with approximately equal proportion of variance explained by SNPs in each of the four MAF bins > 0.1.
ii) When genome-wide similarities based only on SNPs with MAF > 0.4 are fitted 11% (s.e. 1%) of the variance in liability is explained (Supplementary Table 5), with approximately equal proportion of variance explained by SNPs in each of the four MAF bins > 0.1.
iii) None of the MAF bins fitted separately can explain the variance explained when all SNPs are used (**Supplementary Table 5**).

Our simulations were designed to explore if a genetic architecture of only rare variants was consistent with our results. Based on the known relationship between allele frequencies and LD, it is highly unlikely that the variance associated with common SNPs reflects only rare causal variants. For example, the maximum LD r^2 possible between variants of frequency 0.4 and 0.01 is only 0.015. In the simulation where 50% of the variance in liability was associated with SNPs with MAF< 0.1 the

joint analysis across MAF bins and the analysis using only individual bins demonstrate that, as expected from the simulation strategy, SNPs with MAF < 0.1 explained close to the true values of variance in liability allocated to them; the results for MAF < 0.1 therefore are verification of the simulation strategy and are not designed for comparison to the observed results. In contrast, under the assumption that the LD architecture is the same between the SNPs with MAF > 0.1 and SNPs in our analysis with MAF < 0.1 as between SNPs with MAF > 0.1 and all causal variants with MAF < 0.1, then the simulation results for MAF > 0.1 can be compared to the observed results.
The analysis using SNPs with MAF > 0.1 captured only ~36% (0.08/0.25, 0.18/0.5, 0.30/0.80) of the true simulated genetic variance. In particular, in the analyses fitting only individual MAF bins the variance explained decreased as the MAF frequency of the SNP bin increased, so that SNPs with MAF > 0.4, only explained ~10% of the total variance associated with the SNPs with MAF < 0.1, compared to 50% (0.11/0.22) in the PGC-SCZ data. The pattern of results across MAF bins in the simulation shows a decreasing proportion of the variance explained with increasing MAF bins whereas the variance attributed to each MAF was approximately equal in the PGC-SCZ analyses.
For comparison, the simulation in which all causal variants have frequency across the allele spectrum the pattern of the proportion of variance explained by each MAF bin is similar to the observed pattern.

The simulation provides a best-case scenario for a rare variants only model, as the causal variation is associated with SNPs <0.1, extending the boundary of rare to uncommon. It is a best-case scenario for all causal variation being rare, since the average r^2 between the SNPs > 0.1 and causal variation will be greater in our simulation than under the usual definition of a rare variants only model.

4) Comparison of our methods and estimates with those of Purcell et al.[4].
Purcell *et al.* used SNP associations detected in the ISC "discovery" sample to construct a linear predictor (a polygenic score) in the MGS "target" sample; the score explained 0.032 of the variance estimated by Nagelkerke's R^2. This R^2 is on the *observed* scale and is relative to a total *variance of case-control status* of the *target* sample ascertained to have approximately an equal number of cases and controls. In contrast, our estimate of h^2 is on the *liability scale* of the *population* (disease prevalence 1%) and is a direct reflection of the properties of the *discovery* sample. However, the critical difference is that R^2 and h^2 are estimates of different parameters and have different properties. For example, to obtain a high R^2, the estimates of effect sizes of individual SNPs need to be accurate, in contrast our estimate of h^2 is based on a single estimate of genome-wide similarity between all pairs of cases and controls and in this way all causal variants can contribute whatever their true effect size as long as they are in LD with the SNPs included in the analysis. Our estimate of h^2 is an unbiased estimator so that the estimate will not systematically increase or decrease with sample size (although the standard error of the estimate will decrease). In contrast, the polygenic score R^2 will increase with the sample size of the discovery sample, because larger sample size should generate more accurate estimates of each individual SNP effects. The PGC-SCZ analysis[1] showed that using ISC+MGS+Cardiff data sets as a discovery sample generated a Nagelkerke's R^2 of 6% in a target sample comprising the other PGC-SCZ data sets. Purcell *et al.* used simulations to calibrate scenarios of variance in liability against the observed R^2 results. These simulations showed that a proportion of variation in liability in the population in LD with genotyped SNPs of 0.34 was consistent with the polygenic score R^2 of 0.032. It is reassuring that our direct estimate of h^2 is consistent with this simulated calibration analysis (Supplementary Table 2 Analysis 1). The ability of the polygenic score derived from the ISC sample to explain variance in the MGS sample reflects that the same SNPs are associated with schizophrenia in two independent samples; we have directly estimated the correlation in liability between the samples tagged by the SNPs as 0.85 (**Table 2**).

5) Comparison of our method with that of Kang et al[10].

Kang *et al*[10] recently presented the efficient mixed model association expedited method (EMMAX) to account for population structure caused by population stratification and hidden relatedness. The method uses a genome-wide identity-by-state (IBS) similarity matrix in an association framework, to correct for a number of possible confounders in the data, including pedigree relationships, cryptic relationships and stratification. Hence the purpose of fitting the similarity matrix is to soak up 'noise' that might affect association signals between individual SNPs and the phenotype because the residuals in the model for association may be correlated. A similar approach was taken recently for a meta-analysis of multiple sclerosis[11]. Kang *et al.* describe the their model in terms of fitting a kinship matrix (i.e., IBD) but the matrix they fit is an IBS (Balding-Nichols) similarity matrix. The similarity matrix fitted by Kang *et al.* estimated from the SNP data is similar to ours and also similar to that used in Eigenstrat[12]. The variance component that is estimated in the Kang *et al.* implementation is an unknown composite of variation due to pedigree relationships (IBD) and due to LD (IBS).

Kang *et al.* called the proportion of total phenotypic variance explained by fitting the IBS matrix 'pseudo-heritability', but the interpretation of their estimate is not obvious. For example, by including relatives in the analysis (Kang *et al*. are likely to have had close relatives in their examples for quantitative traits because the data were from isolated populations in Finland and Sardinia), the SNP matrix estimates approximate identity-by-descent between close relatives (instead of IBS for distant relatives), and therefore the variance explained is driven by the phenotypic correlation of close relatives. Essentially this is like fitting an 'A (additive) E(environmental)' pedigree based model to the data.

In their application of case-control data, Kang *et al*. also use a linear model (like we do) but because their interest was in SNP-disease association, they did not transform the estimate of the variance component to a different scale nor adjust for ascertainment.

In contrast, our approach is to be extremely stringent on SNP and sample QC and estimated relatedness, so that we minimize or avoid possible confounders and are left over with conventionally unrelated individuals whose phenotypes are only correlated due to the proportion of the genome that they share, so that the estimate of variance reflects LD between unknown 'causal' variants and the genotyped SNPs. In Yang *et al.* (2010, NG) we show that our model is statistically equivalent to fitting all SNPs in the model of analysis (as in a GWAS) but with the SNP effects being random and drawn from a distribution of effects.

In summary, operationally the two methods are similar but the rationale, the interpretation of estimated variance components and the treatment of case-control data differ.

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The following authors are included under International Schizophrenia Consortium (ISC) in the Schizophrenia Psychiatric Genome Wide Association Study Consortium (PGC-SCZ):

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